

EXERCISE-INDUCED OXIDATIVE STRESS AND ANTIOXIDANT DEFENSE IN ATHLETES: MECHANISMS, BIOMARKERS, AND IMPLICATIONS FOR PERFORMANCE AND RECOVERY: A NARRATIVE REVIEW

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To Cite This Article:

EXERCISE-INDUCED OXIDATIVE STRESS AND ANTIOXIDANT DEFENSE IN ATHLETES: MECHANISMS, BIOMARKERS, AND IMPLICATIONS FOR PERFORMANCE AND RECOVERY: A NARRATIVE REVIEW (A. A. Abbas, Trans.). (2026). *International Journal of Advance Research in Education & Literature* (ISSN 2208-2441), 12(5), 1-14. <https://doi.org/10.61841/k75whc69>

ABSTRACT

Background: Muscular contraction increases the production of reactive oxygen and nitrogen species (ROS/RNS). Since the first reports in the late 1970s, exercise-induced oxidative stress has been reconceptualized from an unavoidable by-product of aerobic metabolism to a regulated signalling process that is required for training adaptation, while excessive or prolonged oxidant exposure remains capable of damaging lipids, proteins and DNA.

Objective: To synthesize mechanistic, biomarker and applied evidence on exercise-induced oxidative stress and antioxidant defense in athletes, with particular emphasis on how exercise type and intensity shape redox responses, how these responses relate to muscle damage, recovery and performance, and what this implies for antioxidant supplementation and recovery strategies.

Main content: Contracting skeletal muscle generates ROS through NADPH oxidases, mitochondria, xanthine oxidase and infiltrating phagocytes. Endogenous enzymatic (superoxide dismutase, catalase, glutathione peroxidase, peroxiredoxins) and non-enzymatic (glutathione, vitamins C and E, urate) systems keep these oxidants within a physiological range. Acute exercise transiently increases circulating markers of lipid, protein and DNA oxidation in proportion to the combined intensity and volume of the bout, whereas regular training up-regulates antioxidant enzymes and attenuates subsequent oxidative responses. Endurance, resistance, high-intensity interval and team-sport activities produce distinct time-courses of oxidative stress and muscle damage, typically peaking within 24–72 h. Redox-sensitive pathways—particularly the Nrf2–Keap1 axis and PGC-1 α —link exercise-induced ROS to mitochondrial biogenesis and antioxidant gene expression, and randomized trials show that chronic high-dose vitamin C and E supplementation can blunt these adaptations. Biomarker interpretation is complicated by assay specificity, sampling time and large inter-individual (“redox individuality”) variation.

Conclusion: Exercise-induced oxidative stress is best understood as a dose-dependent hormetic stimulus. Physiological ROS levels drive adaptation and are required for optimal muscle function, whereas excessive or insufficiently recovered training loads shift the balance toward oxidative damage, delayed recovery and impaired performance. Indiscriminate high-dose antioxidant supplementation is not supported; a food-first approach, targeting of documented antioxidant deficiencies, and periodization of any supplementation around adaptation-critical training phases are recommended.

KEYWORDS: Exercise; Oxidative Stress; Reactive Oxygen Species; Antioxidants; Athletes; Nrf2; Biomarkers; Muscle Damage; Recovery; Sports Nutrition

ABBREVIATIONS

8-OHdG, 8-hydroxy-2'-deoxyguanosine; CAT, catalase; CK, creatine kinase; CWI, cold-water immersion; GPx, glutathione peroxidase; GR, glutathione reductase; GSH, reduced glutathione; GSSG, oxidized glutathione; HIIT, high-intensity interval training; LDH, lactate dehydrogenase; MDA, malondialdehyde; NAC, N-acetylcysteine; NF- κ B, nuclear factor kappa B; NOX, NADPH oxidase; Nrf2, nuclear factor erythroid 2-related factor 2; OSI, oxidative stress index; PGC-1 α , peroxisome proliferator-activated receptor gamma coactivator 1-alpha; Prx, peroxiredoxin; RNS, reactive nitrogen species; ROS, reactive oxygen species; SOD, superoxide dismutase; TAC, total antioxidant capacity; TBARS, thiobarbituric acid reactive substances; TOS, total oxidant status; XO, xanthine oxidase.

INTRODUCTION

EXERCISE AND ATHLETIC PERFORMANCE

Systematic training is the principal means by which athletes improve performance. Endurance training increases mitochondrial content, capillary density and oxidative enzyme activity in skeletal muscle; resistance training increases myofibrillar protein content and force-generating capacity; and high-intensity interval training (HIIT) produces a hybrid stimulus that improves both oxidative and glycolytic capacity in a time-efficient manner. Each of these adaptations is the outcome of repeated perturbations of cellular homeostasis followed by recovery, and it is now clear that reactive oxygen species (ROS) generated during contraction are among the signals that translate mechanical and metabolic stress into adaptive gene expression [1–3].

REACTIVE OXYGEN AND NITROGEN SPECIES

“Reactive oxygen species” is an umbrella term for oxygen-derived molecules that are produced as a normal attribute of aerobic life. The superoxide anion radical ($O_2^{\bullet-}$) and hydrogen peroxide (H_2O_2) are the principal redox-signalling agents; H_2O_2 at nanomolar concentrations reversibly oxidizes cysteine thiols on specific protein targets, whereas the hydroxyl radical ($\bullet OH$), formed from H_2O_2 in the presence of transition metals, is indiscriminately reactive and predominantly damaging [4,5]. Reactive nitrogen species (RNS) such as nitric oxide ($NO^{\bullet}$) and peroxynitrite ($ONOO^-$) contribute to the same signalling and damage networks. Both resting and contracting skeletal muscle fibres produce ROS and RNS, and their production increases markedly during exercise [1].

OXIDATIVE STRESS: FROM IMBALANCE TO EUSTRESS AND DISTRESS

Oxidative stress is classically defined as an imbalance between oxidant production and antioxidant defense in favour of the former, leading to disruption of redox signalling and/or molecular damage [6]. Contemporary redox biology distinguishes “oxidative eustress”—low, physiological oxidant exposure that supports adaptive signalling—from “oxidative distress”, in which supraphysiological exposure causes oxidation of lipids (lipid peroxidation), proteins (carbonylation, thiol oxidation) and nucleic acids (8-oxo-guanine formation), with consequent cellular dysfunction [4]. This distinction is central to the interpretation of exercise-induced oxidative stress in athletes.

ANTIOXIDANT DEFENSE

Antioxidant defense comprises enzymatic systems—superoxide dismutases (SOD1, SOD2, SOD3), catalase (CAT), glutathione peroxidases (GPx), peroxiredoxins (Prx), thioredoxins and glutathione reductase (GR)—and non-enzymatic molecules including reduced glutathione (GSH), vitamins C and E, uric acid, albumin, bilirubin and coenzyme Q10 [1,7]. Antioxidants do not simply “scavenge” radicals; they modulate oxidant concentrations so that physiological signalling is preserved while damage is minimized, and their actions *in vivo* are context-dependent [8]. The clinical failure of indiscriminate low-molecular-weight antioxidant therapy in chronic disease trials has reinforced the need for mechanistic precision when antioxidants are recommended to healthy, highly trained individuals [9].

AIM OF THIS REVIEW

This narrative review synthesizes current evidence on (i) the sources of ROS during exercise, (ii) the antioxidant defense systems of athletes, (iii) the biomarkers used to quantify oxidative stress and antioxidant status and their limitations, (iv) modality- and intensity-specific redox responses, (v) the relationships between oxidative stress, muscle damage, recovery and performance, (vi) the redox-signalling pathways underlying training adaptation, and (vii) the evidence for and against antioxidant supplementation and other recovery strategies. Throughout, we emphasize the dual—signalling and damaging—nature of exercise-induced ROS.

LITERATURE SEARCH STRATEGY

Because this is a narrative rather than a systematic review, no protocol was registered and no formal risk-of-bias assessment was performed. To make the evidence base transparent, PubMed/MEDLINE, Scopus and Google Scholar were searched from inception to August 2026 using combinations of the terms “exercise”, “training”, “athletes”, “oxidative stress”, “reactive oxygen species”, “redox”, “antioxidant”, “superoxide dismutase”, “glutathione”, “Nrf2”, “biomarker”, “malondialdehyde”, “isoprostane”, “protein carbonyl”, “8-OHdG”, “muscle damage”, “recovery”, “high-intensity interval training”, “resistance training”, “endurance”, “soccer” and “supplementation”. Reference lists of retrieved articles were hand-searched. Priority was given to original human studies, systematic reviews, meta-analyses and consensus statements published between 2020 and 2026, while foundational mechanistic studies and landmark randomized trials from earlier years were retained. Animal and *in vitro* studies were included only where they clarified mechanisms that cannot be studied directly in athletes.

MECHANISMS OF ROS GENERATION DURING EXERCISE

The first demonstration that exercise increases oxidative processes in humans was published in 1978, when expired pentane—an index of lipid peroxidation—rose during exhaustive cycling [10]. Shortly afterwards, electron paramagnetic resonance detected increased free-radical signals in muscle and liver of exhaustively exercised rats [11]. In the decades since, the principal sources of exercise-induced ROS have been progressively clarified (Figure 1; Table 1) [1,12,13].

MITOCHONDRIA

Mitochondria were long assumed to be the dominant ROS source during exercise because oxygen consumption rises 10–20-fold and a small fraction of electrons leaks from the electron transport chain to form superoxide. However, the fraction

of oxygen converted to superoxide is now known to be lower than early estimates suggested and to fall, rather than rise, when mitochondria move from resting (state 4) to actively phosphorylating (state 3) respiration. Consequently, mitochondrial superoxide production per unit of oxygen consumed is lower during contraction than at rest, and mitochondria are unlikely to be the primary source of cytosolic ROS in contracting muscle [13,14].

NADPH OXIDASES

Experimental work using isolated fibres, pharmacological inhibitors and genetic models indicates that NADPH oxidase isoforms—particularly NOX2 located at the sarcolemma and transverse tubules, and NOX4 in mitochondrial and sarcoplasmic-reticulum membranes—are major contributors to superoxide generation during contraction [14]. NOX-derived ROS are produced in a regulated, stimulus-dependent manner and are positioned to modulate calcium handling, glucose uptake and redox-sensitive kinases, which is consistent with a signalling rather than a purely damaging role [2].

XANTHINE OXIDASE

Xanthine oxidase (XO) catalyses the oxidation of hypoxanthine and xanthine to uric acid with concomitant superoxide and H₂O₂ formation. XO activity in human skeletal muscle increases after eccentric exercise and localizes to microvascular endothelium and infiltrating leukocytes, implicating it in the inflammatory phase of muscle damage [15]. In professional cyclists, the XO inhibitor allopurinol attenuated the rise in creatine kinase, aspartate aminotransferase and malondialdehyde during Tour de France stages [16], and in professional soccer players it prevented match-induced increases in markers of skeletal and cardiac muscle damage and lipid peroxidation [17]. Importantly, however, chronic XO inhibition in trained rats also prevented the exercise-induced activation of redox-sensitive signalling and antioxidant enzyme up-regulation, illustrating the trade-off between protection and adaptation that recurs throughout this field [18].

INFLAMMATORY CELLS AND ISCHAEMIA–REPERFUSION

Muscle-damaging exercise—especially eccentric and high-force contractions—triggers infiltration of neutrophils and macrophages that generate ROS via NADPH oxidase and myeloperoxidase as part of the phagocytic oxidative burst; this secondary oxidant load contributes to the delayed peak in oxidative stress markers observed 24–72 h after damaging exercise [19]. A single HIIT session has recently been shown to increase phagocyte oxidative burst activity together with SOD and CAT activity in young professional athletes [20]. In addition, intense isometric or intermittent contractions produce transient regional ischaemia followed by reperfusion, which favours purine catabolism and XO-dependent superoxide generation. Phospholipase A2 activation and auto-oxidation of catecholamines and haem proteins represent additional, quantitatively smaller sources [1].

Table 1: Major sources of reactive oxygen and nitrogen species during exercise

Source	Principal species	Location / trigger	Relevance to athletes	Key references
NADPH oxidases (NOX2, NOX4)	O ₂ ^{•−} , H ₂ O ₂	Sarcolemma, T-tubules, SR and mitochondrial membranes; activated by contraction	Likely dominant regulated source during contraction; signalling role in Ca ²⁺ handling and glucose uptake	[2,14]
Mitochondrial electron transport chain	O ₂ ^{•−} → H ₂ O ₂	Complexes I and III; leak proportionally lower in state 3 than state 4	Contribution during contraction smaller than historically assumed; important at rest and in recovery	[1,13]
Xanthine oxidase	O ₂ ^{•−} , H ₂ O ₂	Endothelium and leukocytes; ischaemia–reperfusion and purine catabolism	Elevated after eccentric and prolonged exhaustive exercise; inhibition reduces damage markers but may blunt adaptation	[15,16,18]
Inflammatory cells (neutrophils, macrophages)	O ₂ ^{•−} , H ₂ O ₂ , HOCl	Infiltrate damaged muscle 24–72 h after damaging exercise	Secondary oxidant load; explains delayed peaks in biomarkers after matches and eccentric work	[19,20]
Nitric oxide synthases	NO [•] , ONOO [−] (with O ₂ ^{•−})	nNOS/eNOS in muscle and endothelium; increased with contraction and shear stress	Vasodilation and signalling; peroxynitrite formation under high superoxide flux	[1,4]
Other (PLA2, catecholamine and haem auto-oxidation)	O ₂ ^{•−} , lipid radicals	Membrane and plasma	Minor quantitative contribution; may amplify lipid peroxidation	[1]

HOCl, hypochlorous acid; nNOS/eNOS, neuronal/endothelial nitric oxide synthase; PLA2, phospholipase A2; SR, sarcoplasmic reticulum.

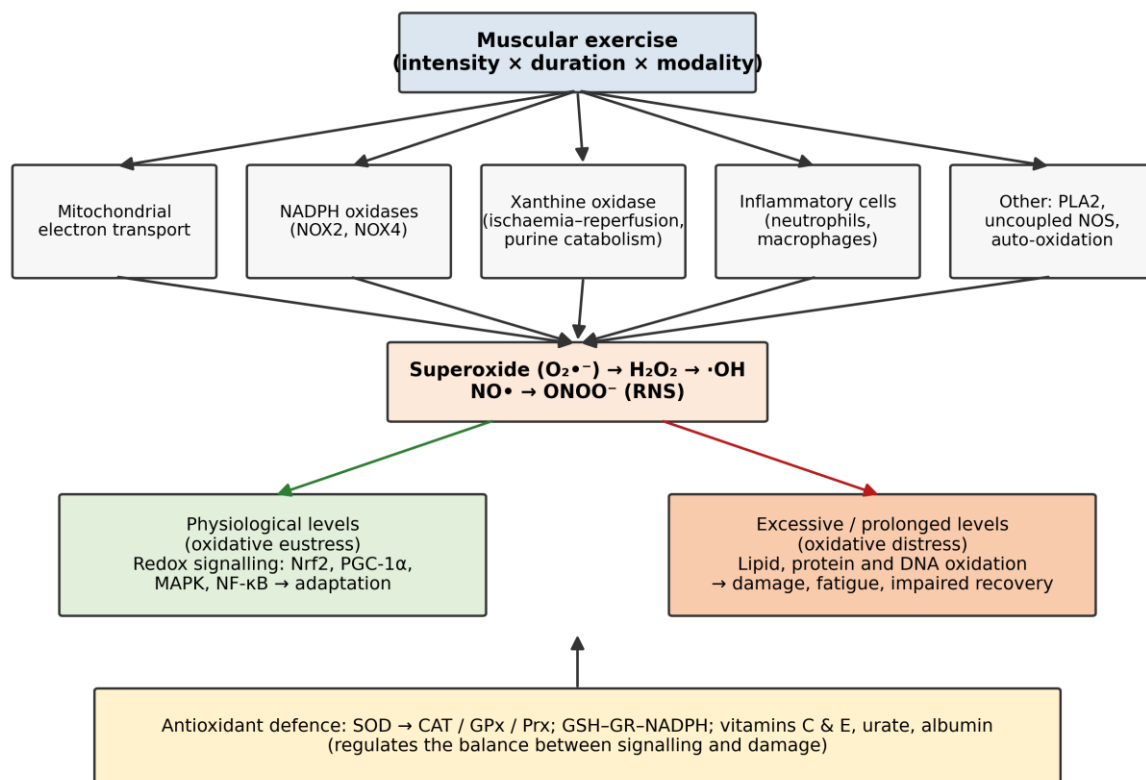


Figure 1: Sources and fates of exercise-induced reactive oxygen and nitrogen species. Muscular exercise activates several oxidant-generating systems whose output is regulated by the enzymatic and non-enzymatic antioxidant network.

At physiological concentrations, oxidants act as signalling molecules (oxidative eustress) that drive adaptation; at excessive or prolonged concentrations they oxidize macromolecules (oxidative distress), contributing to fatigue, muscle damage and impaired recovery.

EXERCISE-INDUCED OXIDATIVE STRESS: ACUTE RESPONSES AND CHRONIC ADAPTATION

ACUTE EXERCISE

A single bout of exercise reliably increases circulating and intramuscular markers of oxidative modification, although the magnitude and timing depend on the marker, the tissue sampled, and the characteristics of the bout and the participant. A meta-analysis of studies in adults concluded that the level of exercise-induced oxidative stress depends not on absolute intensity alone but on the combination of intensity and volume, and that moderate-to-high-intensity aerobic exercise induces substantially larger oxidative responses than ordinary daily activities [21]. A systematic review and meta-analysis of DNA damage after acute aerobic exercise found consistent increases in markers such as 8-OHdG and comet-assay strand breaks, with effect sizes influenced by exercise duration and the timing of sampling [22]. Fitness level modulates these responses: physically active individuals show higher baseline antioxidant capacity and smaller oxidative perturbations after high-intensity exercise than untrained individuals [23].

CHRONIC EXERCISE AND ANTIOXIDANT ADAPTATION

Repeated exposure to exercise-induced ROS is a classic example of hormesis: a stressor that is harmful at high doses produces beneficial adaptation at moderate, intermittent doses [24]. Endurance training increases the activity and protein abundance of SOD2, GPx and, less consistently, CAT in trained muscle, with the magnitude of change depending on training intensity, duration and muscle fibre type [25,26]. These adaptations reduce contraction-induced oxidative damage in trained muscle and are among the mechanisms by which regular exercise protects against oxidative injury in a range of tissues [13]. In humans, even short-term HIIT (three weeks) attenuated post-exercise increases in protein carbonyls and TBARS and improved indices of antioxidant status despite a greater total work output [27]. This phenomenon—exercise-induced antioxidant adaptation—forms the physiological rationale for questioning the routine use of exogenous antioxidants in trained athletes.

ANTIOXIDANT DEFENSE IN ATHLETES

Antioxidant defense operates as a coordinated network rather than as a set of independent scavengers (Figure 3; Table 2).

SUPEROXIDE DISMUTASES

SOD isoforms convert superoxide to H_2O_2 and oxygen. SOD1 (Cu/Zn-SOD) is cytosolic, SOD2 (Mn-SOD) is mitochondrial and SOD3 is extracellular. SOD2 is the isoform most consistently up-regulated by endurance training and its basal muscle content has been associated with maximal oxygen uptake and high-intensity exercise performance in humans [26,28].

CATALASE

Catalase decomposes H_2O_2 to water and oxygen and is concentrated in peroxisomes, with lower activity in skeletal muscle than in liver or erythrocytes. Training-induced changes in muscle catalase are inconsistent, which may reflect its relatively low affinity for H_2O_2 compared with GPx and peroxiredoxins at physiological concentrations [26].

GLUTATHIONE PEROXIDASES AND PEROXIREDOXINS

GPx enzymes reduce H_2O_2 and lipid hydroperoxides using GSH as the electron donor, forming oxidized glutathione (GSSG). Peroxiredoxins, which are highly abundant and kinetically efficient thiol peroxidases, are increasingly recognized as the principal H_2O_2 sensors that transmit oxidant signals to target proteins, so that the same enzymes that remove H_2O_2 also mediate redox signalling [4,7].

THE GLUTATHIONE SYSTEM

GSH is the most abundant low-molecular-weight thiol in muscle. The GSH/GSSG ratio is a widely used index of cellular redox state, and glutathione reductase regenerates GSH from GSSG using NADPH derived largely from the pentose-phosphate pathway. Acute exhaustive exercise transiently lowers blood GSH and raises GSSG, whereas training tends to increase GSH availability and GR activity. Individuals with low baseline glutathione show distinct responses to exercise and to supplementation, a point developed in Section 11 [29].

NON-ENZYMATIC ANTIOXIDANTS

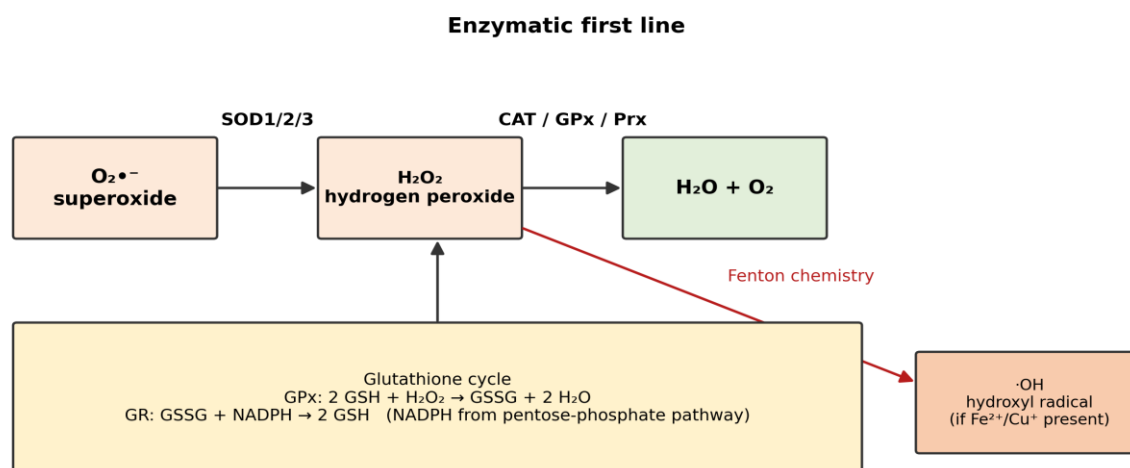
Vitamin C (ascorbate) is the principal aqueous-phase antioxidant and regenerates vitamin E (α -tocopherol), the major lipid-phase chain-breaking antioxidant. Uric acid, the end-product of XO activity, is a quantitatively important plasma antioxidant, which creates the paradox that a marker of oxidant-generating purine catabolism also increases total antioxidant capacity after exercise [30]. Albumin, bilirubin and coenzyme Q10 contribute further capacity. Dietary intake is the primary determinant of vitamin C and E status, whereas urate, albumin and bilirubin are determined largely by endogenous metabolism.

Table 2: Major antioxidant systems relevant to athletes and their interpretation

Antioxidant	Biological role	Location	Response to acute exercise	Response to training	Interpretation in athletes
SOD (SOD1/2/3)	$\text{O}_2^{\bullet -} \rightarrow \text{H}_2\text{O}_2 + \text{O}_2$	Cytosol / mitochondria / extracellular	Variable; transient increase in erythrocytes and muscle	SOD2 increased in trained muscle	First-line enzymatic defence; SOD2 linked to $\text{VO}_{2\text{max}}$
Catalase	$2 \text{H}_2\text{O}_2 \rightarrow 2 \text{H}_2\text{O} + \text{O}_2$	Peroxisomes; erythrocytes	Small or no change	Inconsistent	High-capacity, low-affinity H_2O_2 removal
GPx	H_2O_2 and lipid hydroperoxides $\rightarrow \text{H}_2\text{O}$ / alcohols (GSH-dependent)	Cytosol and mitochondria	Transient increase or decrease depending on GSH availability	Increased with endurance training	Selenium-dependent; key for lipid hydroperoxide removal
Peroxiredoxins / thioredoxin	H_2O_2 sensing and relay to target proteins	Ubiquitous	Rapid reversible oxidation	Up-regulated	Central to redox signalling rather than bulk scavenging
GSH / GSSG, GR	Thiol redox buffer; GR regenerates GSH	All cells; high in erythrocytes and muscle	$\downarrow$ GSH, $\uparrow$ GSSG after exhaustive exercise	$\uparrow$ GSH and GR activity	GSH/GSSG ratio reflects redox state; low baseline GSH identifies responders to NAC
Vitamin C	Aqueous-phase scavenger; regenerates vitamin E	Plasma, cytosol	Transient $\uparrow$ (mobilization) then $\downarrow$	Little change	Dietary; deficiency impairs performance, excess blunts adaptation
Vitamin E	Lipid-phase chain-breaking antioxidant	Membranes, lipoproteins	Minor change	Little change	Dietary; high-dose supplementation not recommended

Antioxidant	Biological role	Location	Response to acute exercise	Response to training	Interpretation in athletes
Uric acid	Plasma scavenger; product of XO	Plasma	↑ after intense exercise	Variable	Confounds TAC; reflects purine catabolism
Albumin, bilirubin, CoQ10	Thiol and lipid-phase support	Plasma, membranes	Minor	Minor	Contribute to TAC; limited specific value

Compiled from references [1,7,26,29,30].



Non-enzymatic support: vitamin C (aqueous), vitamin E (membranes), urate, albumin, bilirubin, CoQ10

Figure 3: The enzymatic antioxidant cascade in skeletal muscle. Superoxide is dismutated by SOD isoforms to hydrogen peroxide, which is removed by catalase, glutathione peroxidases and peroxiredoxins. The glutathione cycle, fuelled by NADPH, regenerates reduced glutathione. In the presence of redox-active iron or copper, unremoved hydrogen peroxide can form the highly damaging hydroxyl radical. Non-enzymatic antioxidants support these systems in aqueous and lipid compartments.

BIOMARKERS OF OXIDATIVE STRESS AND ANTIOXIDANT STATUS IN ATHLETES

Because ROS have half-lives of nanoseconds to seconds, oxidative stress is almost always inferred from stable footprints of oxidative damage, from antioxidant concentrations and enzyme activities, or from composite indices (Table 3) [1,31].

LIPID OXIDATION

Malondialdehyde (MDA), measured either specifically by HPLC or non-specifically as thiobarbituric acid reactive substances (TBARS), is the most frequently reported marker in sports studies, but TBARS lacks specificity and is prone to artefactual formation during sample processing. F2-isoprostanes, prostaglandin-like compounds formed by non-enzymatic peroxidation of arachidonic acid, are widely regarded as the most reliable *in vivo* index of lipid peroxidation and rise reproducibly after prolonged or intense exercise, although their measurement requires mass spectrometry or carefully validated immunoassays [32]. Lipid hydroperoxides and oxidized LDL are additional, less commonly used markers.

PROTEIN AND DNA OXIDATION

Protein carbonyls are relatively stable products of amino-acid side-chain oxidation and increase after high-intensity and eccentric exercise, typically peaking later than lipid markers [27,33]. Oxidative DNA damage is assessed by urinary or plasma 8-OHdG (8-oxo-dG) or by the comet assay in leukocytes; a meta-analysis confirmed a consistent, moderate increase after acute aerobic exercise that resolves within days and is not accompanied by evidence of persistent genomic instability in healthy individuals [22].

GLOBAL INDICES

Total antioxidant capacity (TAC), total oxidant status (TOS) and the derived oxidative stress index (OSI = TOS/TAC) are inexpensive and frequently reported. Their principal limitation is that plasma TAC is dominated by uric acid and albumin, so that post-exercise increases in TAC often reflect purine catabolism rather than improved defense [30]. Enzyme activities (SOD, CAT, GPx) in erythrocytes or plasma are also commonly measured, but their relationship to intramuscular activity is indirect.

METHODOLOGICAL CONSIDERATIONS

Several methodological issues limit inference from athlete biomarker studies. First, blood may not reflect muscle: reactive species are compartmentalized, and plasma markers integrate contributions from many tissues [31]. Second, timing matters: some markers peak immediately after exercise, others at 24–72 h, so single post-exercise samples can miss or misrepresent the response [23,33]. Third, inter-individual variability is large; after the same eccentric protocol, some individuals show oxidative stress while others show reductive stress, a phenomenon termed “redox individuality” that has direct implications for supplementation trials [34]. Finally, a quantitative appreciation of the magnitude of change—not merely statistical significance—is required to judge biological relevance [30]. Multi-marker panels that combine a lipid marker (preferably F2-isoprostanes), a protein marker, a DNA marker and specific antioxidant measures sampled at appropriate time-points are therefore recommended.

Table 3: Commonly used biomarkers of oxidative stress in athletes

Category	Biomarker	Matrix	Typical response to exercise	Strengths	Limitations
Lipid oxidation	F2-isoprostanes	Plasma, urine	↑ after prolonged / intense exercise	Chemically stable; specific; regarded as reference method	Requires MS or validated immunoassay; cost
Lipid oxidation	MDA (HPLC) / TBARS	Plasma, muscle	↑ immediately and/or 24–48 h	Inexpensive; widely used	TBARS non-specific; artefacts during processing
Lipid oxidation	Lipid hydroperoxides, oxLDL	Plasma	↑ acutely	Early products	Unstable; less validated
Protein oxidation	Protein carbonyls	Plasma, muscle	↑, often peaking 24–72 h	Stable; reflects cumulative damage	Non-specific to oxidant species
DNA oxidation	8-OHdG (8-oxo-dG); comet assay	Urine, plasma, leukocytes	↑ moderately after acute aerobic exercise	Reflects genomic oxidative load	Repair kinetics confound; assay variability
Antioxidant status	GSH, GSSG, GSH/GSSG	Erythrocytes, plasma, muscle	↓ GSH / ↑ GSSG acutely	Direct index of thiol redox state	Rapid ex vivo oxidation; handling critical
Antioxidant status	SOD, CAT, GPx activity	Erythrocytes, plasma, muscle	Variable acute; ↑ with training (muscle)	Mechanistic link to defence	Blood activity may not reflect muscle
Antioxidant status	Vitamins C and E; urate	Plasma	Transient changes; urate ↑	Identify deficiencies	Urate confounds TAC
Global indices	TAC, TOS, OSI	Plasma	TAC often ↑ acutely	Cheap; composite	Dominated by urate and albumin; low specificity
Direct detection	EPR / spin trapping	Blood, muscle	↑ acutely	Detects radicals directly	Technically demanding; limited availability

Compiled from references [1,21,22,30–32].

EXERCISE TYPE, INTENSITY AND OXIDATIVE STRESS ENDURANCE EXERCISE

Prolonged running, cycling and swimming impose a sustained increase in oxygen flux and, when very long (marathon, ultra-endurance), progressive glycogen depletion, purine catabolism and low-grade inflammation, all of which increase oxidant production. Endurance events therefore produce among the largest and most prolonged elevations in lipid peroxidation and DNA oxidation markers reported in athletes [21,22]. Against this, endurance-trained athletes display the most robust antioxidant enzyme adaptations, and basal muscle Nrf2, Keap1 and antioxidant enzyme content are associated with endurance and high-intensity performance [26,28].

RESISTANCE TRAINING

Resistance exercise generates ROS through mechanisms that differ from endurance exercise: high-force contractions cause transient ischaemia–reperfusion, eccentric actions produce mechanical disruption of myofibres, and the ensuing inflammatory infiltration adds a secondary, delayed oxidant load [15,19]. Oxidative markers after resistance sessions therefore often peak at 24–72 h rather than immediately post-exercise. Redox signalling is also implicated in hypertrophic adaptation, although in an 11-week trial vitamin C and E supplementation altered acute phosphorylation of p70S6K and MAPK after a strength session without significantly impairing muscle growth, suggesting that the dependence of hypertrophy on ROS signalling is less than that of mitochondrial adaptation [35].

HIGH-INTENSITY INTERVAL TRAINING

HIIT produces a large acute oxidative response at the cessation of exercise that is transient and generally normalized within 24 h, accompanied by a lagging but sustained increase in endogenous antioxidant activity [23]. Repeated exposure rapidly induces adaptation: three weeks of sprint-interval training attenuated post-exercise protein carbonyl and TBARS responses and CK release despite greater work output [27]. In young professional athletes, a single treadmill HIIT session increased SOD and CAT activity without increasing lipid peroxidation, whereas non-athletes showed no significant enzyme response, consistent with training-dependent regulation of the acute antioxidant response [20]. HIIT sessions with substantial eccentric or plyometric content nevertheless cause measurable muscle damage [36].

TEAM SPORTS

Team sports such as soccer, basketball and handball combine repeated sprints, accelerations, decelerations, jumps and changes of direction with a substantial aerobic component. In male professional soccer players, a competitive match increased TBARS, protein carbonyls and uric acid and altered GSH/GSSG for up to 48–72 h, with concurrent 3–8-fold increases in CK and delayed-onset muscle soreness and a 2–17% decline in sprint and jump performance during recovery [33]. Comparable 72-h elevations in MDA, CK and myoglobin were reported by Ascensão and colleagues [37], and inflammatory and performance perturbations followed a similar time-course [38]. In elite female players, a match increased plasma antioxidant concentrations and oxidized glutathione, indicating mobilization of endogenous defenses in the face of increased oxidant flux [39]. Across disciplines, athletes engaged in different sports display distinct baseline redox and inflammatory profiles, which argues against a single “athlete” reference range for redox biomarkers [40,41].

INTENSITY, VOLUME AND THE HORMETIC WINDOW

Taken together, the available meta-analytic evidence indicates that the acute oxidative response scales with the product of intensity and volume rather than with intensity alone [21]. Low-to-moderate loads produce controlled oxidant fluxes that act as signals; well-recovered high-intensity or high-volume loads produce transient oxidative stress that is followed by adaptation; and excessive loads with insufficient recovery produce persistent oxidative stress that is associated with impaired calcium handling, mitochondrial dysfunction and the performance decline characteristic of overtraining [42]. Figure 2 summarizes this model, which frames oxidative stress as a marker of training load that must be interpreted relative to recovery rather than as an outcome to be minimized.

Table 4: Effects of different exercise modalities on oxidative stress and antioxidant defense

Modality	Dominant ROS mechanisms	Typical acute oxidative response	Time-course	Chronic adaptation	Representative evidence
Endurance (running, cycling, swimming)	Sustained O ₂ flux; NOX; mitochondrial; XO with glycogen depletion	Large ↑ F ₂ -isoprostanes, MDA, 8-OHdG proportional to duration	Immediate to 24 h; longer after ultra-endurance	Robust ↑ SOD2, GPx; ↑ Nrf2 targets	[21,22,26]
Resistance / eccentric	Ischaemia–reperfusion; mechanical damage; XO; inflammatory cells	Moderate acute; ↑ protein carbonyls delayed	Peak 24–72 h	Reduced damage response (repeated-bout effect); hypertrophy less ROS-dependent	[15,19,35]
HIIT / sprint interval	High glycolytic flux; NOX; phagocyte burst	Large transient ↑ at cessation; ↑ SOD/CAT in trained	Normalizes within 24 h	Rapid attenuation of oxidative response within weeks	[20,23,27]
Team sports (soccer)	Combination of above; eccentric decelerations	↑ TBARS, carbonyls, urate; ↓ GSH/GSSG	Up to 48–72 h; parallels CK, DOMS, performance loss	Sport-specific baseline redox profile	[33,37,39]

DOMS, *delayed-onset muscle soreness*.

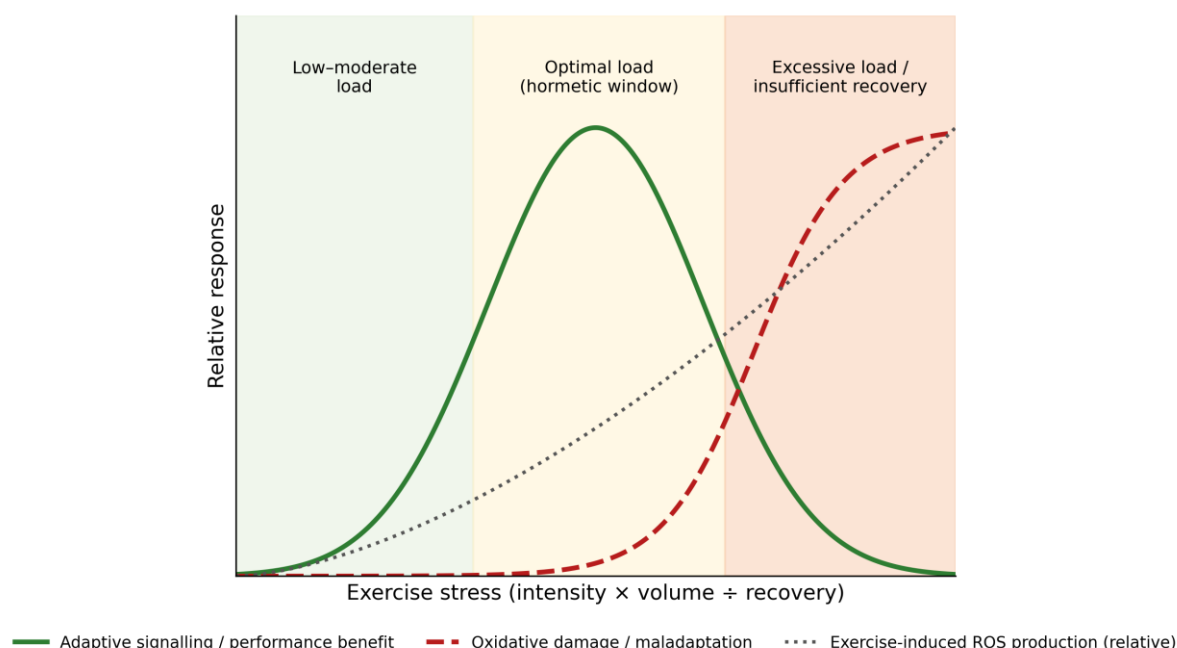


Figure 2: Conceptual relationship between exercise stress, exercise-induced ROS production, adaptive signalling and oxidative damage. Adaptive benefit follows an inverted-U (hormetic) relationship with training load, whereas oxidative damage rises steeply once load exceeds recovery capacity. The position and width of the optimal window differ between individuals and depend on training status, nutrition and recovery.

OXIDATIVE STRESS, MUSCLE DAMAGE AND RECOVERY

Exercise-induced muscle damage and oxidative stress are intertwined but distinct processes. Mechanical disruption of sarcomeres and membranes during damaging exercise releases intracellular proteins into the circulation; creatine kinase (CK), lactate dehydrogenase (LDH) and myoglobin are therefore markers of membrane permeability and myofibre injury, not of oxidative stress per se [43]. The two processes converge because damaged fibres attract phagocytes whose oxidative burst generates ROS, which in turn propagate lipid peroxidation and protein oxidation in adjacent tissue [19]. Consistent with this, the time-courses of CK, oxidative markers, inflammatory cytokines and functional impairment after a soccer match run largely in parallel over 48–72 h [33,38], and XO inhibition reduces both CK release and lipid peroxidation after competition [17].

Recovery from damaging exercise is thus a redox-sensitive, inflammation-dependent process. Interventions that blunt the oxidative-inflammatory phase may accelerate the restoration of function in the short term—an attractive goal during congested competition schedules—but the same phase drives the remodelling that underlies the repeated-bout effect and long-term adaptation. Decisions about anti-oxidative recovery strategies should therefore be made in the context of the athlete's periodized goals (Section 12).

OXIDATIVE STRESS AND ATHLETIC PERFORMANCE: THE DUAL ROLE OF ROS

Skeletal muscle force production depends on an optimal redox state. Experimental data indicate a biphasic relationship in which both excessive reduction and excessive oxidation reduce maximal isometric force, with ROS-mediated oxidation of ryanodine receptors, sarcoplasmic-reticulum calcium ATPase and myofibrillar proteins contributing to reduced calcium release, reduced calcium sensitivity and fatigue during prolonged high-intensity contraction [1,44]. Acute administration of the thiol donor N-acetylcysteine (NAC) has been shown in several trials to delay fatigue during prolonged submaximal exercise, and a meta-analysis found small ergogenic effects that were most evident in exercise lasting longer than a few minutes, with gastrointestinal side-effects at high doses [45]. Conversely, genetic deletion of Nrf2 in mice reduces muscle force and increases fatigue susceptibility, while basal muscle Nrf2 and antioxidant enzyme content in humans are positively associated with $\text{VO}_{2\text{max}}$ and sprint performance [28,46]. These observations illustrate the two faces of ROS in performance: physiological levels are required for optimal contractile function and for the adaptive response to training, whereas excessive levels accelerate fatigue and, when sustained, contribute to the performance decline of overtraining [13,42].

REDOX SIGNALLING AND TRAINING ADAPTATION THE NRF2–KEAP1 PATHWAY

Nuclear factor erythroid 2-related factor 2 (Nrf2) is the master transcriptional regulator of cellular antioxidant and cytoprotective genes. Under basal conditions Nrf2 is bound by Keap1 and targeted for proteasomal degradation; oxidation of Keap1 cysteines by H_2O_2 or electrophiles stabilizes Nrf2, which translocates to the nucleus and activates antioxidant response elements controlling SOD, CAT, GPx, glutathione synthesis, thioredoxin and NADPH-generating enzymes [47]. Acute exercise increases Nrf2 nuclear accumulation in human muscle and peripheral blood mononuclear cells, and

repeated bouts up-regulate Nrf2 targets—an archetypal hormetic mechanism [47,48]. The response appears to be intensity-gated: high- but not low-intensity muscle stimulation activated Nrf2 signalling systemically, including in non-stimulated tissues, implicating a circulating redox-sensitive “exerkine” [49]. Skeletal muscle Nrf2 has also been proposed to confer systemic protection through the release of antioxidant proteins in extracellular vesicles [50]. Proteomic analyses in muscle-specific Nrf2-knockout mice show that training fails to up-regulate hundreds of proteins involved in redox homeostasis and mitochondrial respiration in the absence of Nrf2, and that exercise capacity and fatigue resistance are impaired [46]. Human data linking basal Nrf2/Keap1 expression to performance, and the modulation of this axis by diet and supplements, were recently reviewed [28].

PGC-1A, MITOCHONDRIAL BIOGENESIS AND OTHER PATHWAYS

Exercise-induced ROS also activate redox-sensitive kinases (p38 MAPK, AMPK) and transcription factors (NF- κ B, PGC-1 α) that drive mitochondrial biogenesis, angiogenesis and the expression of heat-shock and antioxidant proteins [2]. The landmark demonstration that vitamin C and E supplementation abolished the exercise-induced increase in PGC-1 α , PGC-1 β , SOD1, SOD2 and GPx1 mRNA and prevented the improvement in insulin sensitivity in humans established that these adaptations are ROS-dependent [51]. Because the same pathways mediate both antioxidant up-regulation and metabolic adaptation, interventions that suppress exercise-induced ROS are predicted to impair both.

ANTIOXIDANT SUPPLEMENTATION: EVIDENCE AND THE ANTIOXIDANT PARADOX

VITAMINS C AND E

Vitamins C and E are the most widely used antioxidant supplements in sport, and the evidence against their chronic high-dose use during training is now substantial. Daily vitamin C (1 g) reduced the training-induced increase in mitochondrial biogenesis markers and endurance capacity in rats and tended to attenuate VO₂max gains in men [52]. Combined vitamin C (1000 mg) and E (400 IU) abolished the exercise-induced expression of PGC-1 α and antioxidant enzymes and the improvement in insulin sensitivity in both untrained and trained men [51]. In an 11-week double-blind randomized trial in 54 recreationally active adults, vitamin C (1000 mg) and E (235 mg) blunted the endurance-training-induced increase in mitochondrial proteins (COX4) and cytosolic PGC-1 α , although VO₂max and running performance improved similarly in both groups over that period [53]. A parallel trial in strength training found altered acute signalling but no significant impairment of hypertrophy [35]. Systematic appraisals conclude that chronic combined high-dose vitamin C and E supplementation should be avoided during periods of heavy training aimed at skeletal-muscle adaptation, whereas evidence that it improves performance or recovery is lacking [7,54,55].

N-ACETYLCYSTEINE, COENZYME Q10, POLYPHENOLS AND OTHER COMPOUNDS

NAC, a cysteine donor that supports glutathione synthesis, is one of the few compounds with reproducible acute ergogenic effects on fatigue resistance, but the effect is small and dose-limited by side-effects [44,45]. Melatonin, vitamin E and α -lipoic acid reduce oxidative-stress markers without convincing performance benefit, while catechins, anthocyanins, coenzyme Q10 and vitamin C may improve vascular function in specific populations without translating into performance gains [7]. Fruit-derived polyphenols (tart cherry, pomegranate, blackcurrant) taken in doses above approximately 1 g of polyphenols per day for at least three days before and after damaging exercise appear to enhance recovery of muscle function through combined antioxidant and anti-inflammatory mechanisms, with some evidence of acute performance benefit [56,57]. Unlike high-dose vitamins, polyphenols act largely as Nrf2 activators and signalling modulators rather than as bulk scavengers, which may explain why they have not been shown to impair adaptation [56]. Selenium and zinc are cofactors for GPx and SOD respectively and should be adequate in the diet, but supplementation above requirements confers no demonstrated advantage and some evidence suggests that selenium and astaxanthin may hamper adaptation [7].

THE ANTIOXIDANT PARADOX AND REDOX INDIVIDUALITY

The apparent paradox—that molecules which reduce oxidative damage can impair the benefits of training—is resolved by recognizing that exercise-induced ROS are required signals. Indiscriminate supplementation dampens the signal, whereas the same supplement may be beneficial in an individual whose antioxidant status is inadequate. In a falsification-design study, targeted vitamin C or NAC supplementation improved performance and redox profile only in individuals screened as deficient in vitamin C or glutathione, respectively, whereas non-targeted supplementation was ineffective; the presence of exercise-induced oxidative stress alone was not a sufficient rationale for supplementation [29]. These findings support a personalized approach in which antioxidant status is measured and supplementation is used to correct documented inadequacy [58]. The IOC consensus statement similarly recommends that supplement decisions follow a complete nutritional assessment and be justified by evidence of deficiency or a specific performance rationale [59].

PRACTICAL SYNTHESIS

- Avoid chronic high-dose combined vitamin C (≥ 1000 mg/day) and vitamin E (≥ 235 –400 mg/day) during training blocks whose aim is mitochondrial or endurance adaptation.
- Screen for and correct documented deficiencies (vitamin C, vitamin E, selenium, zinc, glutathione) rather than supplementing on the basis of oxidative-stress markers alone.
- Consider short-term, food-based polyphenol strategies (e.g., tart cherry, pomegranate) around competition or congested fixtures where rapid recovery outweighs adaptation.

- NAC may be considered acutely before prolonged events in athletes with low glutathione status, with attention to dose and gastrointestinal tolerance.
- Re-evaluate any supplement against sport-specific performance or recovery endpoints, not biomarker changes alone, and within anti-doping constraints on product quality.

NUTRITION AND RECOVERY STRATEGIES

DIET AND OXIDATIVE BALANCE

A food-first approach that supplies adequate energy, carbohydrate, protein and a diverse intake of fruits, vegetables, nuts, seeds and oily fish provides the substrate for endogenous antioxidant systems (cysteine for glutathione, selenium for GPx, zinc and copper for SOD) together with vitamins C and E and polyphenols in physiological amounts and matrices [59,60]. Adequate carbohydrate availability limits reliance on purine catabolism and the associated XO-derived oxidant load during prolonged exercise, and sufficient protein supports the repair of oxidatively modified proteins. Omega-3 fatty acids modulate the inflammatory phase of recovery, although their net effect on lipid peroxidation is complex because polyunsaturated fatty acids are themselves peroxidation substrates. Hydration status influences plasma marker concentrations and should be standardized when biomarkers are monitored.

RECOVERY INTERVENTIONS

Sleep, training periodization with planned recovery days and monitoring of load are the foundations of redox-balanced training; the intramuscular mechanisms of overtraining—including persistent oxidative modification of calcium-handling proteins and mitochondrial dysfunction—underline the importance of recovery rather than pharmacological suppression of oxidative stress [42]. Active recovery after a soccer match did not accelerate the restoration of neuromuscular function compared with passive recovery in elite female players, although it did no harm [61]. Cold-water immersion (CWI) is widely used to reduce soreness and perceived fatigue; however, regular post-exercise CWI attenuated acute anabolic signalling and long-term gains in muscle mass and strength in men undertaking strength training, demonstrating that recovery modalities that suppress the acute inflammatory-oxidative response can carry an adaptation cost [62]. As with antioxidant supplementation, the appropriate question is not whether oxidative stress is reduced but whether the athlete's goal at that point in the season is adaptation or immediate readiness.

SHOULD OXIDATIVE STRESS ALWAYS BE MINIMIZED?

The evidence reviewed here indicates that the answer is no. Exercise-induced oxidative stress is a graded, largely transient and adaptive phenomenon in healthy athletes; prolonged, rigorous exercise does not appear to produce oxidative stress of a magnitude that threatens health in this population [13]. Interventions to reduce oxidative stress are justified when (i) a documented antioxidant deficiency exists, (ii) rapid recovery for repeated competition takes priority over adaptation, or (iii) monitoring indicates persistent oxidative stress consistent with excessive load, in which case the primary corrective is reduced load and improved recovery.

EMERGING CONCEPTS AND FUTURE PERSPECTIVES

Several developments are reshaping the field. First, quantitative redox biology emphasizes the magnitude, compartment and kinetics of specific oxidants rather than composite “oxidative stress” scores, and calls for measurement of H₂O₂ and superoxide with specific probes and identification of their protein targets [5,30]. Second, the recognition of redox individuality has motivated stratified and n-of-1 designs in which baseline antioxidant status determines the intervention [34,58]. Third, Nrf2 biology is moving from rodent models toward human performance phenotypes, with basal Nrf2/Keap1 expression emerging as a candidate determinant of trainability and diet–exercise interactions [28]. Fourth, extracellular vesicles and other exerkines offer a mechanism by which muscle-derived redox signals coordinate systemic adaptation, and may yield accessible biomarkers of adaptive state [50]. Fifth, multi-omics approaches—proteomics of redox post-translational modifications, metabolomics of oxidized lipids and nucleosides—are beginning to define signatures that distinguish adaptive from maladaptive oxidative stress [46]. Finally, integration of biochemical redox panels with wearable-derived load, sleep and heart-rate variability data offers a route to individualized, load-responsive training and nutrition prescription, although validation against performance outcomes is still lacking.

Key research priorities include: (1) standardized, time-resolved biomarker panels using specific markers (F₂-isoprostanes, protein carbonyls, 8-oxo-dG, GSH/GSSG) in athletes across sports; (2) randomized trials of antioxidant strategies stratified by baseline redox status with performance and adaptation as co-primary outcomes; (3) elucidation of the intensity and volume thresholds at which redox signalling transitions to maladaptation in elite populations; (4) sex-specific and age-specific redox responses, which remain under-studied; and (5) the redox effects of established ergogenic aids and recovery modalities.

CONCLUSION

Oxidative stress is not simply a harmful consequence of exercise. Reactive oxygen species generated during muscular contraction—principally by NADPH oxidases, with contributions from mitochondria, xanthine oxidase and infiltrating phagocytes—act as signalling molecules that activate Nrf2, PGC-1 α and related pathways and are required for the antioxidant, mitochondrial and metabolic adaptations that underpin athletic performance. Regular training strengthens endogenous antioxidant defense and attenuates subsequent oxidative responses. When exercise intensity and volume exceed recovery capacity, however, oxidant production can outstrip defense, leading to lipid, protein and DNA oxidation, accelerated fatigue, prolonged muscle damage and the performance decline of overtraining. Biomarkers of oxidative stress

are informative when specific markers are sampled at appropriate times and interpreted quantitatively and individually. Chronic high-dose antioxidant supplementation blunts training adaptation and is not supported for healthy athletes; a food-first strategy, correction of documented deficiencies, and periodization of any recovery-oriented antioxidant intervention around adaptation-critical training phases represent the current evidence-based approach.

DECLARATIONS

Author contributions: A.A.A. conceived the review, performed the literature search, wrote the manuscript and approved the final version.

Funding: This research received no external funding.

Conflicts of interest: The author declares no conflicts of interest.

Ethical approval: Not applicable (review of published literature).

Data availability: Not applicable.

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